

CLAIMS

1. A cartilage membrane having at least one surface part carrying a composition comprising at least one stimulation molecule which is capable of inducing a signal transduction in chondroblast/chondrocytes resulting in the chondroblast/chondrocytes producing and secreting matrix components which form hyalin cartilage or more specifically hyalin articular cartilage.
2. A cartilage membrane according to claim 1, which is a non-immunogenic, non-toxic, biodegradable membrane.
3. A cartilage membrane according to claims 1 or 2, wherein the membrane material is porous or substantially porous
4. A cartilage membrane according to claim 3, wherein the membrane is a natural or synthetic collagen type I membrane or part thereof.
5. An interface membrane with a first surface part and a second second surface part both carrying a composition comprising at least one stimulation molecule which is capable of inducing a signal transduction in chondroblast/chondrocytes and osteoblasts/osteocytes.
6. An interface membrane according to claim 5, which is a non-immunogenic, non-toxic, biodegradable membrane.
7. An interface membrane according to claims 5 or 6, wherein the membrane material is porous or substantially porous.
8. An interface membrane according to claim 7, wherein the membrane is a natural or synthetic collagen type I membrane or part thereof.
9. A membrane according to any of the claims 1-8, wherein the stimulation-molecule comprising at least one RGD motif.
10. A membrane according to claim 9, wherein the stimulation molecule is a natural or synthetic protein or peptide or a fusion or a mixture thereof.
11. A membrane according to claim 10, wherein the stimulation molecule is selected from the group consisting of collagen proteins such as collagen types II, VI, IX, and XI, proteoglycans such as aggrecans, decorin, fibromodulin and biglycan, and non-collagenous proteins such as cryoprecipitate, fibronectin, vitronectin, fibronogen, fibrillin, kistrin, echistatin, von Willebrand factor, tenascin and anchorin CII.
12. A membrane according to claim 11, wherein the stimulation molecule is selected from the group consisting of collagen type II and fibronectin.
13. A membrane according to claim 12, wherein the stimulation molecule is attached to a support.
14. A method for in vivo repair of cartilage defects in joints in mammals, comprising

10057112.012502

- applying, over a cartilage free cavity (7) of a joint, a cartilage membrane (5) with a first surface part of which facing the cartilage free cavity (7), the first surface part of the cartilage membrane (5) carrying a composition comprising at least one stimulation molecule which is capable of inducing a signal transduction in chondroblast/chondrocytes,
- 5 introducing, in the cartilage free cavity (7) between the cartilage membrane (5), the cartilage (2) and the interface (3), a chondroblast/chondrocyte suspension (8), and;
- joining a portion part of the first surface part of the cartilage membrane (5) to the surrounding articular surface (1) so as to sealingly entrap the chondroblast/chondrocyte suspension (8) in the cartilage free cavity (7) using a sealing portion (6), thereby allowing the chondroblast/chondrocyte suspension (8) to produce and secrete matrix components characteristic for hyalin.
- 10
15. A method according to claim 14, wherein the cartilage membrane is a cartilage membrane according to any of claims 1-4 and the stimulation molecule is a stimulation molecule according to claims 9-13.
- 15
16. A method for in vivo repair of bone and cartilage defects in joints in mammals, such as in osteoarthritic joints, comprising
- applying, over a bone free cavity (23) and under a cartilage free cavity (70) of a joint, an interface membrane (21) with a first surface part (22) facing the bone free cavity (23), the interface membrane (21) first surface part (22) carrying a composition comprising at least one stimulation molecule which is capable of inducing a signal transduction in osteoblast/osteocyte, and the second surface part (26) carrying a composition comprising at least one stimulation molecule which is capable of inducing a signal transduction in chondroblast/chondrocytes,
- 20
- 25 introducing, in the interstice between the interface membrane first surface part (22) and the bone (40), an osteoblast/osteocyte suspension (24),
- joining a portion part of the first surface part (22) of the interface membrane (21) to the surrounding interface surface (30) so as to sealingly entrap the osteoblast/osteocyte suspension (24) in the bone free cavity (23) using a sealing portion (25), thereby allowing the osteoblast/osteocyte suspension (24) to produce and secrete matrix components characteristic for bone tissue;
- 30
- applying, over the cartilage free cavity (70), a cartilage membrane (50) with a first surface part facing the second surface part (26) of the interface membrane (21), the first surface part of the cartilage membrane (50) carries a composition comprising at least one stimulation molecule which is capable of inducing a signal transduction in chondroblast/chondrocytes resulting in the chondroblast/chondrocytes producing and secreting matrix components which form hyalin cartilage,
- 35

10057112.012502

introducing, in the cartilage free cavity (70) between the interface membrane (21), the cartilage membrane (50) and the cartilage (20), a chondroblast/chondrocyte suspension (80),

5 joining a portion part of the cartilage membrane (50) to the surrounding articular surface (10) so as to sealingly entrap the chondroblast/chondrocyte suspension (80) in the cartilage free cavity (70) using a sealing portion (60), thereby allowing the chondroblast/chondrocyte suspension (80) to produce and secrete matrix components which form hyalin.

10 17. A method for in vivo repair of bone and cartilage defects in joints in mammals using arthroscopy, such as in osteoarthritic joints, comprising treating an interface membrane (21) with a first sealing portion component, applying, over a bone free cavity (23) and under a cartilage free cavity (70) of a joint, an interface membrane (21) with a first surface part (22) facing the bone free cavity (23), the interface membrane (21) first surface part (22) carrying a composition comprising at least one stimulation molecule which is capable of inducing a signal transduction in osteoblast/osteocyte, and the second surface part (26), which carries a composition comprising at least one stimulation molecule which is capable of inducing a signal transduction in chondroblast/chondrocytes,

15 introducing, in the interstice between the interface membrane first surface part (22) and the bone (40), an osteoblast/osteocyte suspension (24), joining a portion part of the first surface part (22) of the interface membrane (21) to the surrounding interface surface (30) so as to sealingly entrap the osteoblast/osteocyte suspension (24) in the bone free cavity (23) using a second sealing portion component, thereby allowing the osteoblast/osteocyte suspension (24) to produce and secrete components characteristic for bone tissue;

20 introducing, in the cartilage free cavity (70) between the interface membrane (21), and the articular surface, a chondroblast/chondrocyte suspension (80), thereby allowing the chondroblast/chondrocyte suspension (80) to produce and secrete components characteristic for hyalin.

25 30

18. A method according to claim 16-17, wherein the membranes are membranes according to any of the claims 1-8 and the stimulation molecule is a stimulation molecule according to any of the 9-13.

35 19. A method according to any of claims 14-18, wherein the chondroblast/chondrocyte suspension is a suspension of autologous chondroblast/chondrocytes.

20. A method according any of claims 16-19, wherein the osteoblast/osteocyte suspension is a suspension of autologous osteoblast/osteocyte.

1005712.012502

21. A kit for cartilage repair comprising at least one cartilage membrane according to any of claims 1-4 and at least one stimulation molecule according to claims 9-13.
22. A kit according to claim 21 comprising at least one interface membrane
5 according to claims 5-8.
23. Use of at least one membrane according to claims 1-13 for the preparation of a kit according to claims 21 or 22 for the treatment of a mammal having a cartilage defects or bone and cartilage defects.
24. Method of treatment according to any of the claims 14-20 for the treatment of a
10 mammal having cartilage defects or bone and cartilage defects.
25. A method according to claim 24 wherein the method is used for the treatment of chondral lesions or osteochondral lesions, osteochondritis dissecans (OCD), chondromalacia and osteoarthritis.
26. A method for preparation of chondroblast/chondrocyte or osteocyte/osteoblast
15 suspensions comprising harvesting mesenchymal and/ or mesenchymal precursor cells from a source such as bone marrow, perichondrium, periosteum, blood, blood vessels or muscle;
adding the harvested cells to a cell culture flask comprising at least one growth medium;
20 growing the harvested cells until colony forming units with a cell number size in the ranging order of 10-20.000 cells /clone are formed with fibroblastic phenotype (CFU-f);
transferring the CFU-f cells into a new cell culture flask comprising at least one selection medium for differentiation of the CFU-f's into chondroblast/chondro-
25 cytes, osteocytes/osteoblasts or myoblasts/myotubes;
and harvesting of the differentiated cells.
27. A method according to claim 26, wherein the suspensions are used for the treatment of cartilage and/or bone and cartilage defects in mammals.
28. A method according to claims 26 or 27, wherein the selection medium
30 comprises components more specific for selection than for growth.

1005712.012502